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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant(s): Badley et al. Application No.: 09/554,956 Filed: 7/11/2000 Title: Improvements in or Relating to Displacement Assays Attorney Docket No.: IMIN.P-019	Group Art Unit: 1641 Examiner: G. Gabel

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313

Submission of Appeal Brief

Dear Sir:

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In support of the Appeal in the above-captioned application, Applicants enclose:

(1) an Appeal Brief,

(2) a Request for an Extension of Time, and

(3) a Credit Card Payment form for $725.

The Commissioner is authorized to charge any additional fees or credit any overpayment to Deposit Account No. 15-0610.

Respectfully submitted,

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I hereby certify that this paper and any attachments named herein are transmitted to the United States Patent and Trademark Office, Fax number: 703-872-9306 on May 24, 2005.

Marina T. Larson, PTO Reg. No. 32,038

May 24, 2005
Date of Signature

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant(s): Badley et al.	
Application No.: 09/554,956	
Filed: 7/11/2000	Group Art Unit: 1641
Title: Improvements in or Relating to Displacement Assays	Examiner: Gailene Gabel
	Confirmation No.: 6821
Attorney Docket No.: IMIN.P-019	

BRIEF FOR APPELLANT

This brief is filed in support of Applicants' Appeal from the final rejection mailed September 21, 2004. Consideration of the application and reversal of the rejections are respectfully urged.

Real Party in Interest

The real party in interest is Inverness Medical Switzerland GmbH, which is a subsidiary of Inverness Medical Innovations, Inc.

Related Appeals and Interferences

To Applicants knowledge, there are no related Appeals or Interferences.

Status of Claims

Claims 1-3, 5-16 and 22 are pending in this application. Claims 4 and 17-21 have been canceled. Claims 23 and 24 were present in the original PCT application, but were canceled during International prosecution.

I hereby certify that this paper and any attachments named herein are transmitted to the United States Patent and Trademark Office, Fax number: 703-872-9306 on May 24, 2005.

Marina T Larson

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Status of Amendments

All amendments have been entered.

Summary of Claimed Subject Matter

The present application relates to a method for detecting the presence of an analyte of interest in a sample. Exemplary analytes are antibodies, nucleic acids and hormones. (Page 4, lines 5-11) As set forth in independent claim 1, the first step of the claimed method is providing a first surface that has a displaceable moiety reversibly immobilised thereon. (Page 3, last partial paragraph, Page 4, last paragraph) The displaceable moiety has an affinity for the first surface that is lower than the affinity of the displaceable moiety for the analyte of interest. (Page 5, lines 9-16) When a sample containing the analyte of interest is placed in contact with the first surface, the analyte specifically displaces the displaceable moiety from the first surface. (Page 3, last partial paragraph)

After the displaceable moiety is released, the displaceable moiety displaced from the first surface is caused to contact a second surface bearing a capture moiety which specifically binds to the displaceable moiety, so as to capture the displaceable moiety on the second surface. (Page 3, last line, to Page 4, line 3). The capture moiety and the displaceable moiety may be members a specific binding pair, such an as antigen/antibody or hormone/receptor pair (Page 4, lines 17-22).

When the displaceable moiety is captured by the capture moiety at the second surface, the capture generates a detectable signal. ((Page 4, line 3) This signal is detected by means other than Surface Plasmon Resonance. Examples of suitable detection means are evanescent or acoustic wave sensors to detect changes in weight of the sensor or to cause a fluorescent emission (Page 7, lines 12-15; Page 7, line 26-Page 8, line 5), the inhibition of an on-going reaction that results in a detectable color change (Page 7, lines 18-25); and the modulation of an electrochemical property of the capture moiety. (Page 8, lines 6-16).

In the method as claimed, the detectable signal is not generated unless and until the displaceable moiety is captured on the second surface, whereupon said detectable signal

indicating detection of analyte in said assay is generated." (Page 6, lines 13-21) This feature is distinguished from a signal generating molecule that is inherently capable of generating a signal, whether or not it is released from the first binding means, and where the act of capture plays no part in the process of signal generation. (Page 2, lines 7-12).

Grounds of Rejection to be reviewed on Appeal

Claims 1-3, 7-10 and 12-16 stand rejected under 35 USC § 102(b) as anticipated by US Patent No 5,281,539 of Schramm.

Claim 11 stands rejected under 35 USC § 103(a) as unpatentable over Schramm in view of US Patent No. 5,082,630 of Partin et al.

Claims 5, 6, and 22 stand rejected under 35 USC § 103(a) as unpatentable over Schramm in view of US patent No. 6,025,166 of Presta et al.

Argument

I. Claims 1-3, 7-10 and 12-16 are not anticipated by US Patent No 5,281,539 of Schramm

Anticipation requires that a single reference disclose each and every element of the claimed invention, and that the elements be arranged as in the claims. Claim 1, upon which all of the rejected claims depend, requires the generation and detection of a signal. However, as specified in the claim, "the detectable signal cannot be generated unless and until the displaceable moiety is captured on the second surface." Applicants submit that this limitation is not met by Schramm, and therefore that the anticipation rejection is in error.

The Schramm reference generally relates to systems that use signal generating molecules such as enzymes or fluorescent molecules which can be captured without deletion of the signal generating ability. (Col. 4, lines 63-67). These are the types of molecules distinguished in the present invention, and by their very description, they have signal generating capability which is not dependent on the occurrence of capture. Unlike all of the other embodiments of Schramm,

which depend on the capture of signal-generating molecules, Fig. 7 states that Sensor 1 (44) and Sensor 2 (46) may be electrodes such as Clark electrodes. (Schramm, Col. 8, lines 34-35).

A. *Schramm is not enabling as to Fig. 7*

In order to be anticipatory, the reference relied upon must provide an enabling disclosure. Schramm does not meet this standard with respect to the embodiment of Fig. 7 on which the Examiner relies. In the embodiment described in Fig. 7, the sensors are said to be electrodes such as Clark electrodes. Clark electrodes are oxygen electrodes,[1] and they would not directly detect anything that is bound to the sensor surface, nor appear to have anything to do with the device as disclosed in Schramm. Further, there is no description of how a signal is generated in this system using a Clark electrode, and how the signal depends on the binding of the displaceable moiety to surface of Sensor 2. To the extent that the electrode may be some other type of electrode, this is not disclosed nor is the type of signal measured (current, potential, resistance, etc) between the electrodes, nor how it would be determined. Thus, there is no enablement of this embodiment, and thus there can be no anticipation.

B. *Schramm fig. 7 does not disclose generating a species capable of generating a detectable signal*

The Examiner has not explained, and Applicants submit that there is no evidence that capture of conjugate 30" at sensor 2 in Schramm Fig. 7 results in the formation of a species capable of producing a detectable signal. In the Office Action of September 21, 2004, the

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[1] As defined on one web site, a Clark electrode is "An oxygen electrode consisting of the tip of a platinum wire exposed to a thin film of electrolyte covered by a plastic membrane permeable to oxygen but not to water or the electrolyte. When a certain voltage is applied, oxygen is destroyed at the platinum surface; the flow of current is then proportional to the rate at which oxygen can diffuse to the platinum surface from the gas or liquid sample outside the membrane, and is thus a measure of the oxygen pressure in the sample; commonly used to measure oxygen pressure in arterial blood samples." http://www.books.md/C/dic/Clarkelectrode.php

Examiner states that "the displaceable moiety 'species' generated in Sensor 2 is capable of producing its distinct detectable signal separate from that in sensor 1," but the basis for this argument is unclear. To the extent that Fig. 7 of Schramm is understandable, it appears that a single signal is generated based on the difference between Sensor 1 and Sensor 2. The conjugate 30" is capable of generating this signal, or of modulating this signal whether it is bound at Sensor 1 or Sensor 2. Thus, there is no basis for a conclusion that the binding of conjugate to Sensor 2 produces a species that it itself capable of generating a detectable signal, and claim 1 is not anticipated. The rejection of claim 1 and all of the claims dependent thereon should therefore be reversed.

C. *Claim 2 is not anticipated*

Claim 2 specifies that the displaceable moiety is an "immunoglobulin molecule or an antigen-binding derivative thereof." In Schramm, the component of the assay that would correspond to this displaceable moiety is the conjugate 30". The conjugate 30" is described in Schramm as a "molecular conjugate of the analyte with a signal generating moiety" (Col. 3, lines 62-64), and states that this may be an enzyme covalently bound to the analyte (Col. 5, lines 9-11.) There is no disclosure of a displaceable moiety that is an immunoglobulin, and therefore claim 2 is not anticipated.

D. *Claim 3 is not anticipated*

Claim 3 specifies that the displaceable moiety is an "bispecific antibody or bispecific antigen-binding antibody derivatives." In Schramm, the component of the assay that would correspond to this displaceable moiety is the conjugate 30". The conjugate 30" is described in Schramm as a "molecular conjugate of the analyte with a signal generating moiety" (Col. 3, lines 62-64), and states that this may be an enzyme covalently bound to the analyte (Col. 5, lines 9-11.) There is no disclosure of a displaceable moiety that is a bispecific antibody, and therefore claim 3 is not anticipated.

E. *Claims 8 and 22 are not anticipated*

Claim 8 is dependent on claim 7. Taking the limitations of the claims together, claim 8 requires that "the first surface comprises a plurality of intervening molecules which bind relatively loosely to the displaceable moiety, such that the binding affinity of the intervening molecules for the analyte of interest is greater than that of the displaceable moiety for the intervening molecules, and that the intervening molecule is an analogue of the analyte of interest." There is no disclosure in Schramm of an analyte-analogue being bound to Sensor 1 in any of the embodiments. Rather, the first binding means 26" (the one on Sensor 1) has an affinity for binding the analyte. (Col. 3, lines 61-62). Thus, claim 8 is not anticipated, nor is claim 22 which depends from claim 8.

F. *Claim 12 is not anticipated*

Claim 12 states that capture of the displaceable moiety by the capture moiety directly modulates an electrochemical property of the capture moiety, which modulation comprises the detectable signal. The Examiner states that "when using electrodes to detect the detectable signal, the analyte, if present, continually displaces the displacable moiety and then is continually captured by the capture antibody so that the measured signal from the sensors each continualy and individually changes with the concentration of analyte in the sensors." (Office Action of 9/21/2004, page 4). As pointed out above, this is incorrect, because the electrodes act as a pair, producing one signal. Furthermore, nothing in this explanation shows any modification of an electrochemical property of the capture moiety which is what is required by claim 12. For example, the capture moiety is not oxidized or reduced, nor is its redox potential said to be changed.

II. Claim 11 is not obvious over Schramm in view of Partin

The Examiner has rejected claim 11 has obvious over the combination of Schramm and Partin (US Patent No. 5,082,630). Partin discloses a fiber optic which has an immobilized

antibody and a labeled antigen on its surface. The labeled antigen is displaced by analyte, and a decrease in fluorescence is detected. The Examiner states that

> "Partin is incorporated with the teaching of Schramm only for the teaching of a detectable signal generated by an acoustic or evanescent wave wherein if the analyte if bound analyte is present in the sample, the analyte molecules displace some of the bound, fluorescent tagged derivatives, resulting in a decrease (modulation) in signal detected by a detecting diode."

(Office Action of September 21, 2004, Page 6). Applicants submit that this argument is flawed for several reasons.

First, as the examiner's comments intimates, claim 11 requires that "the detectable signal comprises the generation of, or the modulation of, an evanescent or acoustic wave." The Examiner has not indicated where in Partin there is any disclosure of an evanescent or acoustic wave. These types of waves are modulated by changes in the mass of the detector, not in fluorescence. (Specification Page 7, lines 10-15). Thus, the relationship of Partin to claim 11 is unclear.

Furthermore, to the extent using an optical fiber as one or both of the supports in Schramm would be deemed obvious, this would not apply to the embodiment of Fig. 7 which is the one the examiner has relied upon in other rejections since there the detection is done using electrodes not fluorescent reagent. The other embodiments of Schramm, however, do not meet the limitations of the present claims because a fluorescently-labeled reagent is capable of producing a signal at any time it is irradiated, and does not meet the limitation of claim 1 (on which claim 11 depends) that "the detectable signal cannot be generated unless and until the displaceable moiety is captured on the second surface.

III. Claims 5, 6 and 22 are not obvious over Schramm in view of Presta

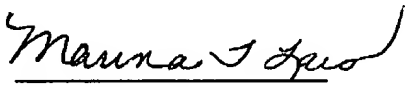
The Examiner rejected claims 5, 6 and 22 under 35 USC § 103 as obvious over Schramm in view of Presta (US Patent No. 6,025,166). Claims 5 and 6 respectively define the displaceable moiety as a fusion protein or a mimotope which is an analogue of the analyte. Claim 22 depends on claims 7 and 8 and defines the intervening moiety as a mimotope. The Examiner cites Presta for a teaching of fusion proteins, and argues that the use of mimotopes

would have been obvious. Thus, Presta does nto overcome the fundamental deficiencies of the Schramm reference. Accordingly, these claims should be allowed for the same reasons discussed above with respect to the anticipation rejection.

Conclusion

For the foregoing reasons, Applicants submit that all of the claims on Appeal are allowable. Reversal of the rejections is respectfully urged.

Respectfully submitted,



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Claims Appendix

1. A method of detecting the presence of an analyte of interest in a sample, the method comprising the steps of:

providing a first surface having reversibly immobilised thereon a displaceable moiety, the displaceable moiety being immobilised on the first surface, said displaceable moiety having an affinity for the first surface lower than the affinity of the displaceable moiety for the analyte of interest;

exposing the first surface to a sample comprising the analyte of interest, whereby the analyte of interest specifically displaces the displaceable moiety from the first surface;

causing the displaceable moiety displaced from the first surface to contact a second surface bearing a capture moiety which specifically binds to the displaceable moiety, so as to capture the displaceable moiety on the second surface, said capture generating a species capable of producing a detectable signal; and

treating the species capable of producing a detectable signal to generate said signal and detecting the signal; wherein said detection is performed by means other than Surface Plasmon Resonance, and wherein the detectable signal cannot be generated unless and until the displaceable moiety is captured on the second surface.

2. A method according to claim 1, wherein the displaceable moiety comprises an immunoglobulin molecule or an antigen-binding derivative thereof.

3. A method according to claim 1, wherein the displaceable moiety comprises a bispecific antibody or bispecific antigen-binding antibody derivatives.

5. A method according to claim 1, wherein the displaceable moiey comprises a fusion protein.

6. A method according to claim 1, wherein the displaceable moiety comprises a mimotope which is an analogue of the analyte of interest.

7. A method according to claim 1, wherein the first surface comprises a plurality of intervening molecules which bind relatively loosely to the displaceable moiety, such that the binding affinity of the intervening molecules for the analyte of interest is greater than that of the displaceable moiety for the intervening molecules.

8. A method according to claim 7, wherein the intervening molecule is an analogue of the analyte of interest.

9. A method according to claim 1, wherein the capture moiety comprises an immunoglobulin molecule or an antigen-binding variant thereof.

10. A method according to claim 1, wherein the displaceable moiety and the capture moiety comprise members of a specific binding pair.

11. A method according to claim 1, wherein the detectable signal comprises the generation of, or the modulation of, an evanescent or acoustic wave.

12. A method according to claim 1, wherein the capture of the displaceable moiety by the capture moiety directly modulates an electrochemical property of the capture moiety, which modulation comprises the detectable signal.

13. A method according to claim 1, wherein the first and second surfaces are provided on separate respective first and second supports.

14. A method according to claim 1, wherein the first and second surfaces are provided on a single support.

15. A method according to claim 1, wherein the first and/or second surface is provided on a solid support which is planar, particulate or porous.

16. A method according to claim 1, wherein the analyte of interest is selected from the group consisting of steroid hormones, protein hormones, nucleic acids, peptides, bacterial and viral antigens, and immunoglobulins.

22. A method according to claim 8 wherein the intervening molecule is a mimotope of the analyte of interest.

Evidence Appendix

none

Related Proceedings Appendix

none